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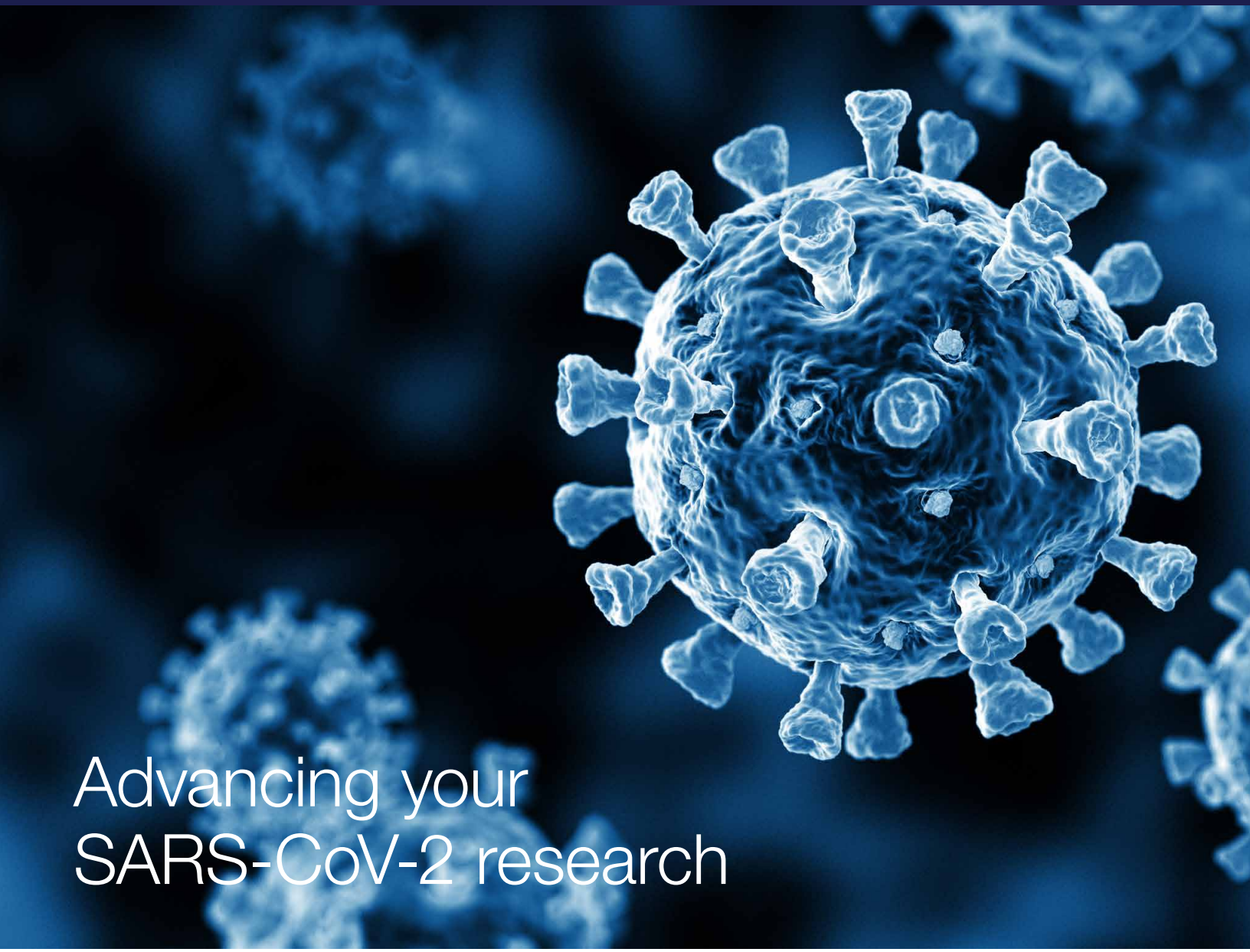
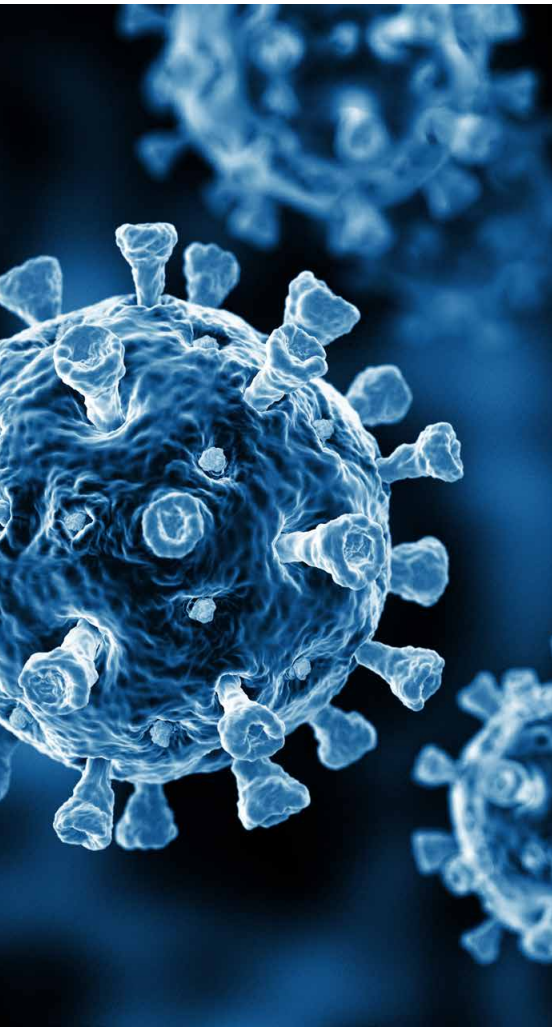


Advancing your SARS-CoV-2 research

TaqMan qPCR solutions for studying the biology and pathogenesis of SARS-CoV-2

ThermoFisher SCIENTIFIC

Contents



End-to-end qPCR solutions for pathogen biology research

SARS-CoV-2 is a novel virus in humans, and there are many unknowns about the viral lifecycle and pathogenesis. Studying pathogen biology and virus–host interactions is critical to understanding molecular pathogenesis, identifying relevant biomarkers, and developing future antiviral therapeutics.

Thermo Fisher Scientific offers qPCR solutions specifically designed for infectious disease research, including a robust library of predesigned Applied Biosystems™ TaqMan® Gene Expression Assays targeting specific genes, pathways, and disease sets. TaqMan Assays contain everything you need, including Applied Biosystems™ TaqMan® MGB probe and PCR primer sets pre-mixed and formulated to work right out of the box. No additional design, optimization, or melt curve analysis is needed. Advanced primer/probe sequence selection criteria plus MGB probe enhancement deliver the specificity and reproducibility you need to help ensure confidence that your results are generated from target amplification—not non-specific dye binding. For optimal results, complement TaqMan Assays with application-specific Applied Biosystems™ TaqMan® master mixes.

Simplify your workflow with Applied Biosystems™ TaqMan® flexible array panels

Looking at a large set of genes in a pathway, disease, or biological process is an efficient way to identify markers of interest. Our flexible-content panels offer an easy way to select a relevant combination of assays in the format that matches your experiment. We have designed several flexible panels specifically for SARS-CoV-2 research that address the most cited genes related to entry and restriction factors as well as cytokines, chemokines, and growth factors. Each panel starts with a curated list of predesigned TaqMan Gene Expression Assays preloaded into our easy-to-use online configurator, which allows you to modify the panel as needed to meet your research requirements. Easily add or delete assays, modify the layout, or change the selected controls. Flexible panels save time and effort by giving you the versatility and control of a custom-designed panel without the need to identify the appropriate assays from scratch.

Choose the format that best suits your experimental needs:

Single-tube assays in a variety of sizes

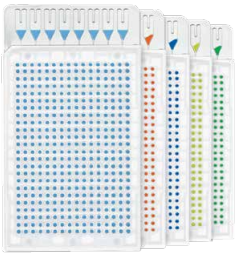
96-well plates:

- 0.2 mL
- 0.1 mL

384-well plates*

* Flexible panels are available in 384-well plates through our Specialty Plating service.

384-well Applied Biosystems™ TaqMan® Array Cards



High-throughput Applied Biosystems™ OpenArray™ technology

Viral entry factors

SARS-CoV-2 manipulates host factors to enable each phase of its life cycle, including viral entry. Elucidating the molecules and signaling pathways implicated in SARS-CoV-2 entry is key to understanding infectivity and tissue-specific tropism, pathogenesis, and immune evasion. As an essential step in the SARS-CoV-2 life cycle, viral entry is also a prime target for potential therapeutic intervention.

Coronavirus entry requires specific binding of the spike (S) protein to cellular entry receptors, followed by cleavage of the S protein by host proteases. While both SARS-CoV and SARS-CoV-2 use angiotensin-converting enzyme 2 (ACE2) as a receptor [1,2], virus-specific interactions with host cofactors are a critical determinant in viral entry, infectivity, and tissue tropism. Researchers have identified a variety of cofactors that facilitate entry of SARS-CoV-2 [1,3], including cell-surface serine proteases TMPRSS2 and TMPRSS4 [4], and neuropilin-1 (NRP1) [5]. RNA expression analysis demonstrates that these host cofactors are differentially expressed in human tissues [3], indicating flexibility and redundancy in cofactor utilization. Further research into viral entry is needed to understand differential infectivity of viral variants, elucidate the molecular mechanisms of tissue-specific pathology, and identify potential therapeutic targets.

The **Applied Biosystems™ TaqMan® Coronavirus Entry Factor Flexible Array Panel** targets 13 genes involved in the attachment of SARS-CoV-2 and other associated coronaviruses to the host cells. The panel also contains three positions for additional targets of interest and/or candidate endogenous controls.

Current endogenous controls, PPIA and GAPDH, were chosen due to their stable expression levels [6].

Available for multiple species (human, mouse, or rat), and in these formats: 96-well plates (0.1 and 0.2 mL), TaqMan Array Cards, and OpenArray technology.

Target genes:

ACE2, TMPRSS2, TMPRSS4, TMPRSS11A, TMPRSS11B, BSG, ANPEP, CLEC4G, FURIN, CTSL, CTSB, DPP4, NRP1

Controls:

- PPIA, GAPDH
- SDHA: optional control, not included on panel
- 18S: standard as manufacturing control

TaqMan Coronavirus Entry Factor Flexible Array Panel

Platform	Configuration	Cat. No.	Array ID	Species
TaqMan Array Card	16	4346798	RTZTEGZ	Human
TaqMan Array Plate, 96-well, 0.2 mL	16	4413264	RAH49YX	Human
TaqMan Array Plate, 96-well, 0.1 mL	16	4413261	RPFVKWR	Human
OpenArray technology	18	4471124	RVDJZJC	Human
TaqMan Array Card	16	4346798	RT2W72X	Mouse
TaqMan Array Plate, 96-well, 0.2 mL	16	4413264	RAMFW4T	Mouse
TaqMan Array Plate, 96-well, 0.1 mL	16	4413261	RPGZFGN	Mouse
OpenArray technology	18	4471124	RVEPR39	Mouse
TaqMan Array Card	16	4346798	RT322MV	Rat
TaqMan Array Plate, 96-well, 0.2 mL	16	4413264	RANKRPP	Rat
TaqMan Array Plate, 96-well, 0.1 mL	16	4413261	RPH492K	Rat
OpenArray technology	18	4471124	RVFVKN6	Rat

Viral restriction factors

Restriction factors are antiviral effector molecules produced by the host cell to inhibit early viral replication and propagation. Expression of host restriction factors can be induced via interferons (IFNs), important mediators in innate immune response. SARS-CoV-2 is shown to be inhibited by Type I IFNs [7,8], suggesting that interferon-stimulated genes (ISGs) and host restriction factors play an important role in antiviral defense [9].

Researchers have identified various ISGs that show broad antiviral activities against SARS-CoV-2, including restricting virus entry, inhibiting viral RNA synthesis, and blocking viral translation [10]. For example, the ISGs cholesterol 25-hydroxylase (CH25H) and lymphocyte antigen 6 complex, locus E (LY6E) both potentially restrict cellular infection by interfering with membrane fusion and viral entry [11,12]. Zinc finger antiviral protein (ZAP), which specifically targets CpG 5 dinucleotides in viral RNA sequences, is also shown to restrict SARS-CoV-2 [13]. Ultimately, a comprehensive analysis is required to identify the molecular effectors of SARS-CoV-2 inhibition and the molecular mechanisms that contribute to variable pathogenesis.

The **Applied Biosystems™ TaqMan® Coronavirus Restriction Factor Flexible Array Panel** targets 13 genes shown to interfere with various steps involved in the life cycle of SARS-CoV-2 and other associated coronaviruses. The panel also contains three positions for additional targets of interest and/or candidate endogenous controls.

Current endogenous controls, PPIA and GAPDH, were chosen due to their stable expression levels [6].

Available for multiple species (human, mouse, or rat), and in these formats: 96-well plates (0.1 and 0.2 mL), TaqMan Array Cards, and OpenArray technology.

Target genes:

LY6E, IFITM1, IFITM2, IFITM3, ZAP/ZC3HAV1, BST2, CLEC4D, ELF1, REC8, IFIT3, DNAJC6, ZBP1, CH25H

Controls:

- PPIA, GAPDH
- SDHA: optional control, not included on panel
- 18S: standard as manufacturing control

TaqMan Coronavirus Restriction Factor Flexible Array Panel

Platform	Configuration	Cat. No.	Array ID	Species
TaqMan Array Card	16	4346798	RTRWE2U	Human
TaqMan Array Plate, 96-well, 0.2 mL	16	4413264	RAWCWKF	Human
TaqMan Array Plate, 96-well, 0.1 mL	16	4413261	RTTZ9MR	Human
OpenArray technology	18	4471124	RVAAAEH	Human
TaqMan Array Card	16	4346798	RTTZ9MR	Mouse
TaqMan Array Plate, 96-well, 0.2 mL	16	4413264	RAXGP6D	Mouse
TaqMan Array Plate, 96-well, 0.1 mL	16	4413261	RPMFW7N	Mouse
OpenArray technology	18	4471124	RVCE3YF	Mouse
TaqMan Array Card	16	4346798	RTFVK2F	Rat
TaqMan Array Plate, 96-well, 0.2 mL	16	4413264	RAPRKAU	Rat
TaqMan Array Plate, 96-well, 0.1 mL	16	4413261	RA9HH6V	Rat
OpenArray technology	18	4471124	RVH49U2	Rat

Cytokines, chemokines, and growth factors

Cytokines, chemokines, and growth factors are signaling molecules that regulate host immune responses. Identifying the molecular mechanisms of different immune responses is critical to understanding host susceptibility and SARS-CoV-2 pathogenesis [9–12].

In response to SARS-CoV-2, a variety of immune pathways involved in inflammation, oxidative stress, and antiviral T cell responses are dysregulated. In severe cases of coronavirus, a proinflammatory cytokine storm, including IL-1, IL-6, IL-12, IFN-γ, and TNF-α, is an indicator of poor prognosis [14–16]. There is evidence that SARS-CoV-2 also perpetuates hyperinflammation via suppression of the antioxidant NRF2 gene expression pathway [17]. While a robust T cell response is required to control early immune responses, dysregulated T cell activation has negative associations [18]. Understanding the immune signaling pathways involved in SARS-CoV-2 will elucidate the beneficial and detrimental effects of the host immune response and guide future research for potential biomarkers and therapeutics.

The **Applied Biosystems™ TaqMan® Coronavirus Immune Signaling Flexible Array Panel** targets a portfolio of 29 cytokines, chemokines, and growth factors involved in the immune response to SARS-CoV-2 and other coronaviruses. The panel also contains three positions for additional targets of interest and/or candidate endogenous controls.

Current endogenous controls, PPIA and GAPDH, were chosen due to their stable expression levels [6].

Available for multiple species (human, mouse or rat), and in these formats: 96-well plates (0.1 and 0.2 mL), TaqMan Array Cards, and OpenArray technology.

Target genes:

IL1B, IL2, IL4, IL5, IL6, IL7, IL10, IL12, IL13, IL16, IL18, IFNB1, IFNg, TNF, TGFB1, M-CSF/CSF1R, MIF, VEGF, SCGF, HGF, TRAIL/TNFSF10, CCL2, CCL3/MIP1a, CCL5, CCL11, CCL27, CXCL1, CXCL10, CXCL12

Controls:

- PPIA, GAPDH
- SDHA: optional control, not included on panel
- 18S: standard as manufacturing control

TaqMan Coronavirus Immune Signaling Flexible Array Panel

Platform	Configuration	Cat. No.	Array ID	Species
TaqMan Array Card	32	4346799	RTYMJXF	Human
TaqMan Array Plate, 96-well, 0.2 mL	32	4391528	RA322F2	Human
TaqMan Array Plate, 96-well, 0.1 mL	32	4413259	RPRWEXF	Human
OpenArray technology	56	4471125	RVDJXJD	Human
TaqMan Array Card	32	4346799	RTCE4CM	Mouse
TaqMan Array Plate, 96-well, 0.2 mL	32	4391528	RA9HH6U	Mouse
TaqMan Array Plate, 96-well, 0.1 mL	32	4413259	RPWCWM7	Mouse
OpenArray technology	56	4471125	RVEPR4A	Mouse
TaqMan Array Card	32	4346799	RTDJXWJ	Rat
TaqMan Array Plate, 96-well, 0.2 mL	32	4391528	RAAAAJJ	Rat
TaqMan Array Plate, 96-well, 0.1 mL	32	4413259	RPXGP74	Rat
OpenArray technology	56	4471125	RVFVKN7	Rat

Host genetic factors

The broad spectrum of clinical manifestations resulting from SARS-CoV-2 infection, as well as the association of risk factors such as advanced age and preexisting health conditions with severe disease, highlight the importance of identifying host genetic components that contribute to susceptibility and severity of infection. These determinants include single-nucleotide polymorphisms (SNPs) and deletions or duplications in host genes that alter expression of key SARS-CoV-2 entry factors or host immune response molecules, although other genetic factors may also play roles. Initial studies comparing cohorts of patients with severe disease to control groups have uncovered assoications with SNPs in *ACE2* and *TMPRPSS2* and severe outcomes [1–3]. Additionally, genome-wide association studies have linked clusters containing SNPs in *OAS* genes, *IFNR2*, and *TYK2* with the risk of hospitalization [4]. Researchers also identified potential associations between severe disease with variants of *TLR7*, *IFITM3*, major histocompatibility complex (MHC) class I, and *APOE* genes [5].

As additional associations between host SNPs and severe disease are identified, further research is required to characterize the molecular mechanisms underlying these associations. This research will enable risk stratification for individuals with specific genetic backgrounds, inform research management and future therapy selection, and may guide public health policies.

Applied Biosystems™ TaqMan® SNP Genotyping Assays for SARS-CoV-2 host genetics research

The Applied Biosystems™ TaqMan® host genetic factors panel contains assays for 37 SNPs that have been associated with SARS-CoV-2 disease severity, curated directly from published studies. Each SNP assay utilizes gold-standard TaqMan Assay chemistry to discriminate between the wild-type and variant alleles. Each assay is available as a single tube or can be customized as part of 96- or 384-well TaqMan array plates or cards by contacting **Specialty_Plates@thermofisher.com**.

Download the complete list of assays at

TaqMan Assay host genetic factors set

Gene symbol	dbSNP ID	Reference
ABO	rs657152_a_c	doi: 10.1056/NEJMoa2020283
ABO	rs657152_a_t	doi: 10.1056/NEJMoa2020283
ACE1	rs1799752	doi: 10.3390/ijms21103474 doi: 10.1183/23120541.00940-2020
ACE2	rs4240157	doi: 10.1101/2020.06.18.20135152
ACE2	rs6632680	doi: 10.1101/2020.06.18.20135152
ACE2	rs1476524	doi: 10.1101/2020.06.18.20135152
ACE2	rs2048683	doi: 10.1101/2020.06.18.20135152
ACE2	rs2106809	doi: 10.3389/fped.2020.00206 doi: 10.1007/s13577-021-00489-0
ACE2	rs233575	doi: 10.1186/s13578-020-00519-8 doi: 10.1016/j.jmii.2020.04.015
ACE2	rs2074192	doi: 10.1093/ajh/hpaa223
ALOXE3	rs147149459	doi: 10.1016/j.virusres.2020.198163
APOE	rs429358	doi: 10.1093/gerona/glaa131 doi: 10.1186/s40246-020-00290-4
APOE	rs7412	doi: 10.1093/gerona/glaa131
BRF2	rs138763430	doi: 10.1016/j.virusres.2020.198163
CCHCR1	rs143334143	doi: 10.1038/s41586-020-03065-y
CCR2	rs6808074	doi: 10.1101/2020.12.01.407429
DPP9	rs2109069	doi: 10.1038/s41586-020-03065-y
ERAP2	rs150892504	doi: 10.1016/j.virusres.2020.198163
HLA-G	rs9380142	doi: 10.1038/s41586-020-03065-y
IFITM3	rs12252	doi: 10.1186/s40246-020-00290-4
IFNAR2	rs2236757	doi: 10.1038/s41586-020-03065-y
IFNAR2	rs2284551	doi: 10.1101/2020.12.01.407429
LZTFL1	rs73064425	doi: 10.1038/s41586-020-03065-y
LZTFL1	rs71325088	doi: 10.1038/s41586-020-03065-y
NOTCH4	rs3131294	doi: 10.1038/s41586-020-03065-y
OAS1	rs2057778	doi: 10.1101/2020.12.01.407429
OAS1	rs6489867	doi: 10.1038/s41586-020-03065-y
OAS3	rs2010604	doi: 10.1101/2020.12.01.407429
OAS3	rs10735079	doi: 10.1038/s41586-020-03065-y
TMEM181	rs117665206	doi: 10.1016/j.virusres.2020.198163
TMEM189–UBE2V1	rs6020298	doi: 10.1038/s41421-020-00231-4
TMRPSS2	rs12329760	doi: 10.1186/s40246-020-00290-4 doi: 10.1186/s12916-020-01673-z doi: 10.1101/2021.03.04.21252931
TMRPSS2	rs2070788	doi: 10.1016/j.bbrc.2020.05.179
TMRPSS2	rs464397	doi: 10.1016/j.bbrc.2020.05.179
TMRPSS2	rs469390	doi: 10.1016/j.bbrc.2020.05.179
TYK2	rs74956615	doi: 10.1038/s41586-020-03065-y
TYK2	rs11085727	doi: 10.1038/s41586-020-03065-y

Targeting individual genes

If you need to focus on just a few or even a single gene, we offer predesigned TaqMan Assays in a single-tube format. These are available for any of the gene targets included in the flexible array panels, plus pro-inflammatory and cytotoxic mediators.

Predesigned TaqMan Assays consist of a forward primer, one or more TaqMan probes, and a reverse primer premixed and optimized for the specific gene of interest. These assays provide the ability to obtain fast, reliable, and accurate results with off-the-shelf assay kits rather than laboriously designing and optimizing your own.

Want to do more than gene expression? Assay solutions include SNP genotyping, copy number variation, and miRNA applications as well. TaqMan Assays are designed using a robust probe/primer design pipeline and verified using up-to-date annotations and gold-standard TaqMan Assay chemistry. That is why predesigned assays are backed by our performance guarantee—promising they will work as described or we will credit or replace them.*

Viral entry factors	Restriction factors	Cytokines	Pro-inflammatory and cytotoxic mediators		Chemokines and receptors	Additional targets
ACE2	BST2	IL1B	GNLY	KLRD1	CCL2	HGF
ANPEP	CH25H	IL2	GZMA	M-CSF	CCL3	IFIT1
BSG	CLEC4D	IL4	GZMB	MIF	CCL5	IFNGR1
CLEC4G	DNAJC6	IL5	GZMK	PRF1	CCL11	IFNGR2
CTSB	ELF1	IL6	IFNB1	TGFB1	CCL20	IFT43
CTSL	IFIT3	IL7	IFNG	TGFB2	CCL27	ISG15
DPP4	IFITM1	IL8	KLRB1	TNF	CCR1	KRT4
FURIN	IFITM2	IL10	KLRC1	TNFSF10	CCR5	KRT7
NRP1	IFITM3	IL12	KLRC2		CXCL1	SCGF
TMPRSS11A	LY6E	IL13			CXCL10	STAT1
TMPRSS11B	REC8	IL16			CXCL12	VEGF
TMPRSS2	ZAP / ZC3HAV1	IL18			CXCL3	
TMPRSS4	ZBP1				CXCL9	

* Terms and conditions apply. See full details of the guarantee at **thermofisher.com/taqmanguarantee**.

Custom assay design

For researchers wanting to design their own primer and probe sets to identify a novel target or proprietary sequence, for example, we have two options for you.

Custom TaqMan Assays

Use the Applied Biosystems™ TaqMan® Custom Assay Design Tool (CADT) to design a formulated assay from your primer and probe sequences. You will tap into the same robust assay design pipeline utilized by our predesigned TaqMan Assays. Simply select your bioinformatic analysis and assay specificity preferences and enter your target sequence. Sequence submissions are completely confidential; we will not share your target sequences or assay sequences with any third parties.

If you do not have a predefined input sequence, the CADT will help you search for sequences by keyword (gene symbol, accession number, etc.) or by genomic location in a broad range of the most popular and well-studied model species, including human, mouse, pig, dog, cow, and Arabidopsis.

Find the TaqMan Custom Assay Design Tool at **thermofisher.com/cadt**

Custom primers and probes

If you prefer to design your own assay with separate primer and probe components, we offer a full portfolio of dual-labeled Applied Biosystems™ TaqMan® probes and unlabeled oligos for use as qPCR primers. Whether you want to simultaneously interrogate multiple targets, use your own bioinformatics to design a probe, or detect exotic targets that do not have a predesigned assay, we offer the ideal probes to design your own assay. Custom Applied Biosystems™ TaqMan® MGB (minor groove binder) Probes and Applied Biosystems™ TaqMan® QSY Probes deliver outstanding performance and are manufactured using the same facilities and raw materials as the TaqMan Assays featured in over 200,000 publications.

Custom MGB probes—MGB probes offer the best all-around combination of sensitivity, precision, and specificity. MGB technology enables shorter probe designs, resulting in maximal sequence discrimination and target flexibility, and are best for detecting up to two targets within the same reaction.

Custom QSY probes—QSY probes are best-suited for multiplexed detection of more than two targets and pair with Applied Biosystems™ ABY™ and Applied Biosystems™ JUN™ dyes, which are optimized for Applied Biosystems™ instruments.

Multiplexing with TaqMan probes

The multiplexing capabilities of TaqMan probes enable cost savings and conservation of limited samples, and provide even more flexibility for your real-time PCR assay designs.

MGB probes labeled with Applied Biosystems™ FAM™ and Applied Biosystems™ VIC™ dyes can be combined with our proprietary ABY and JUN dyes and QSY probes to allow amplification of up to four targets in a single reaction.

All four dyes are optimized for the filter sets on Applied Biosystems™ real-time PCR instruments and work together with minimal spectral overlap for optimal performance.

Sequence detection primers

Sequence detection primers are high-quality, unlabeled oligos for use with either TaqMan probes or Applied Biosystems™ SYBR™ dye for all of your real-time PCR research applications. These primers come desalted, are available in your choice of scales, and are shipped in liquid or dried-down form. Sequence detection primers are synthesized using the same raw materials and carefully controlled processes as our TaqMan probes, enabling consistency and quality in every batch.

Explore the full range of custom primers and probes at **thermofisher.com/customprobes**

Maximize performance with the right master mix

TaqMan chemistry provides industry-recognized gold-standard performance, so pairing TaqMan Assays with a TaqMan master mix helps you bring the highest sensitivity, specificity, and reproducibility to your qPCR research. Choose the mix that's right for your experiment.

Applied Biosystems™ TaqMan® Fast Advanced Master Mix

- Optimized for TaqMan Gene Expression Assays
- <40 min run time
- Formulated for multiplexing
- 72-hour benchtop stability
- Compatible with a wide range of real-time PCR instruments

Applied Biosystems™ TaqMan® Fast Virus 1-Step Master Mix

- 1-step formula supports qPCR cycling in <30 min
- Tolerant of inhibitors
- High-throughput capability
- Single-tube, 4X formulation

Discover the full portfolio of reagents at **thermofisher.com/mastermix**

Employ the full Applied Biosystems qPCR ecosystem for ultimate performance and efficiency

While any of our assays and reagents can be used as stand-alone solutions, combining the performance of Applied Biosystems™ TaqMan® reagents with the power of Applied Biosystems™ QuantStudio™ real-time PCR systems brings ultimate flexibility and efficiency to your qPCR workflow.

QuantStudio real-time PCR systems detect changes in gene expression as low as 1.5-fold. The systems support a broad range of genomic applications, such as analyses of gene expression, microRNAs and noncoding RNAs, copy number variation, drug metabolism enzymes, and protein expression; SNP genotyping; and mutation detection.

A user-friendly touchscreen and intuitive software make the systems easy to operate. Designed to reduce contamination and increase productivity, several QuantStudio real-time PCR systems include remote setup, monitoring, and data sharing. The Applied Biosystems™ QuantStudio™ 6 and 7 Pro Real-Time PCR Systems also feature hands-free commands.

Whether your system requires low, medium, or high throughput (or all three in a single instrument), multiplexing capability, or full remote connectivity, there is a QuantStudio™ instrument that meets your needs.

Take a look at the full QuantStudio lineup at **thermofisher.com/quantstudio**

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